

AMENDMENTS TO THE SPECIFICATION

Please amend page 9, lines 14-16 as shown below.

Examples of the halogen atom represented by R¹ or R³ group or that may be present therein in the present specification include fluorine, chlorine, bromine, and iodine.

Please amend page 11, lines 20-25 as shown below.

The reaction is usually performed in a solvent. Examples of the solvent include, for example, the same solvent as described. Any suitable amount of the solvent may be used and it is usually from 0.5 to 100 parts by weight, preferably from 1 to 30 parts by weight per 1 part by weight of the 1-[(4-chlorophenyl)phenylmethyl]-4-(tert-butoxycarbonyl)piperazine 4-(tert-butoxycarbonyl)piperazine of formula (1).

Please amend page 13, lines 23-29 as shown below.

The solvent that may be used to recrystallize the optically active adduct salt of 4-(tert-butoxycarbonyl)piperazine compound of formula (3) can be selected, for example, from a solvent as mentioned above depending on the salt to be crystallized. Any suitable amount of the solvent may be used, and is usually from 0.5 to 100 parts by weight, preferably from 1 to 30 parts by weight per 1 part by weight of the adduct salt of 1-[(4-chlorophenyl)phenylmethyl]piperazine 4-(tert-butoxycarbonyl)piperazine compound of formula (3).

Please amend page 14, lines 1-21 as shown below.

The solution of the adduct salt of 1-[(4-chlorophenyl)phenylmethyl]piperazine 4-(tert-butoxycarbonyl)piperazine compound of formula (3) is usually prepared at a temperature that is not higher than the boiling point of the solution and ranges usually from 0 to 120°C, preferably approximately from 20 to 100°C.

The solution containing the adduct salt of 1-[(4-chlorophenyl)phenylmethyl]piperazine 4-(tert-butoxycarbonyl)piperazine compound of formula (3) is typically cooled to precipitate the desired adduct salt at a temperature that is not lower than the freezing point of the solution and ranges usually from -80 to 50°C, preferably approximately from -50 to 30°C.

The solvent that has insufficient solubility with respect to the adduct salt may be selected, for example, from a solvent having a lower polarity such as aliphatic or aromatic hydrocarbon showing insufficient solubility to the crystals to be purified at a precipitating temperature depending on the crystals. The amount thereof is not particularly limited and is usually from 0.5 to 100 parts by weight, preferably from 1 to 30 parts by weight per 1 part by weight of the optically active adduct salt of 1-[(4-chlorophenyl)phenylmethyl]piperazine 4-(tert-butoxycarbonyl)piperazine compound of formula (3).

After the recrystallization, the precipitated adduct salt of optically active 1-[(4-chlorophenyl)phenylmethyl]piperazine 4-(tert-butoxycarbonyl)piperazine compound of formula (3) can be isolated readily by a conventional method, for example, by filtration.

Please amend page 15, line 11-29 to page 16, line 1, as shown below.

The reaction is usually performed in a solvent. Examples of the solvent include, for example, the same solvent that may be used in the reaction of the optically active acid and 1-[(4-chlorophenyl)phenylmethyl]piperazine 4-(tert-butoxycarbonyl)piperazine compound of formula (3). The solvent may be used in an amount of from 0.5 to 100 parts by weight, preferably from 1 to 30 parts by weight per 1 part by weight of the adduct salt of 1-[(4-chlorophenyl)phenylmethyl]piperazine 4-(tert-butoxycarbonyl)piperazine compound of formula (3).

The reaction can be carried out by mixing the adduct salt of the optically active 4-(tert-butoxycarbonyl)piperazine compound of formula (3) and a base; followed by phase separation using water and the water immiscible organic solvent, thereby removing the optically active acid and the base that may be present in the organic layer.

The reaction is usually conducted at a temperature range of from -50 to 100°C, preferably approximately from 0 to 50°C.

After completion of the reaction, the obtained optically active 4-(tert-butoxycarbonyl)piperazine compound of formula ~~(1)~~ (1') can be used in a solution form as it is for the subsequent reaction. The product may also be isolated by distillation of the solvent, or may be isolated by crystallization under cooling in a solvent, followed by filtration to collect the precipitated crystallized product.

Please amend page 16, lines 3-23 as shown below.

Removal of the tert-butoxycarbonyl group of the obtained optically active 4-(tert-butoxycarbonyl)piperazine compound of formula ~~(1)~~ (1') can be accomplished readily by allowing the compound to react with an acid to produce the optically active 1-[(substituted phenyl)phenylmethyl]piperazine of formula (7) or the adduct salt of optically active 1-[(substituted phenyl)phenylmethyl]piperazine of formula (6).

Examples of the acid include, for example, an inorganic acid such as hydrogen chloride, hydrogen bromide, sulfuric acid, or the like, and an organic acid such as methansulfonic acid, trifluoroacetic acid, acetic acid, formic acid or the like.

Any amount of the acid may be used, for example, a catalytic amount of the acid may be used, and the amount is preferably from 0.1 to 50 moles, preferably from 1 to 30 moles per mol of the optically active 4-(tert-butoxycarbonyl)piperazine compound of formula (1).

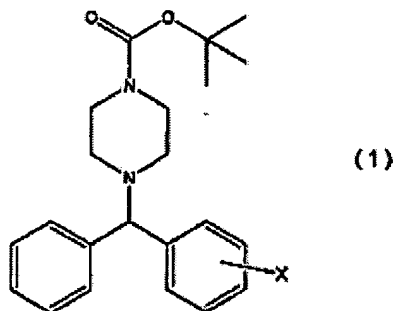
Examples of the solvent that may be used include, for example, the same solvent as used for the reaction of the optically acid (2) and 4-(tert-butoxycarbonyl)piperazine compound. Any amount of the solvent may be used and it is preferably used in an amount from 0.5 to 100 parts by weight, preferably from 1 to 30 parts by weight per 1 part by weight of the optically active 4-(tert-butoxycarbonyl)piperazine compound of formula ~~(4)~~ (1').

Please amend page 17, lines 4-11 as shown below.

The optically active 1- [(substituted phenyl)phenylmethyl]piperazine of formula (7) can be produced by adding a base, for example, in a form of an aqueous base solution, followed extraction with water immiscible organic solvent, phase separation, thereby removing the acid that may be present, and then removing the solvent by distillation. The product may be crystallized or precipitated by cooling the organic solvent solution, and the precipitated crystals can be collected by filtration.

Please amend the present Abstract of the Disclosure as shown below.

A method for producing 1-[(substituted phenyl)phenylmethyl]piperazines useful as intermediates for pharmaceuticals and the like, more particularly, for example, to an intermediate for the production of antiallergic pharmaceuticals. A 4-(tert-butoxycarbonyl)piperazine compound of ~~formula (1)~~ formula (1):



wherein X denotes a chlorine atom, a C1-C3 alkyl group or a C1-C3 alkoxy group, and an optical isomer present therein.